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EFFECT OF A-STRAIN. DIASTEREOSELECTIVE SYNTHESIS OF 3,2'-METHYLENE BRIDGED CIS-4a-ARYLDECAHYDROISOQUINOLINE RING SYSTEM VIA N-ACYLIMINIUM ION-POLYENE RING CLOSURE

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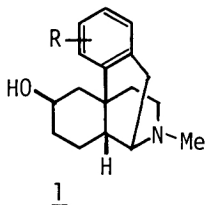
Diastereoselective synthesis of 3,2'-methylene bridged 6-oxygenated 4a,6-cis-4a,8a-cis-4a-aryldecahydroisoquinoline ring system was achieved by an application of N-acyliminium ion-polyene cyclization at the initial stage.

Biomimetic polyene cyclizations have been applied to the synthesis of multicyclic compounds with excellent stereocontrol.[1,2] Polyene cyclizations by using N-acyliminium ion as a cationic initiating center[3] have also been applied to a synthesis of N-polycyclic compounds in a stereocontrolled manner.[4] As a part of our general investigations on the N-acyliminium ion-polyene cyclizations,[5] we investigated a synthesis of a new tetracyclic isoquinoline ring (2), a positional isomer of isomorphinan ring system (1) with regard to benzyl methylene bridge, by an application of an N-acyliminium ion-polyene cyclization at the initial stage. The results of our studies are herein described.



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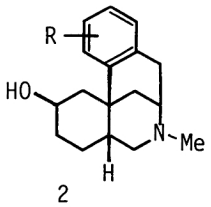
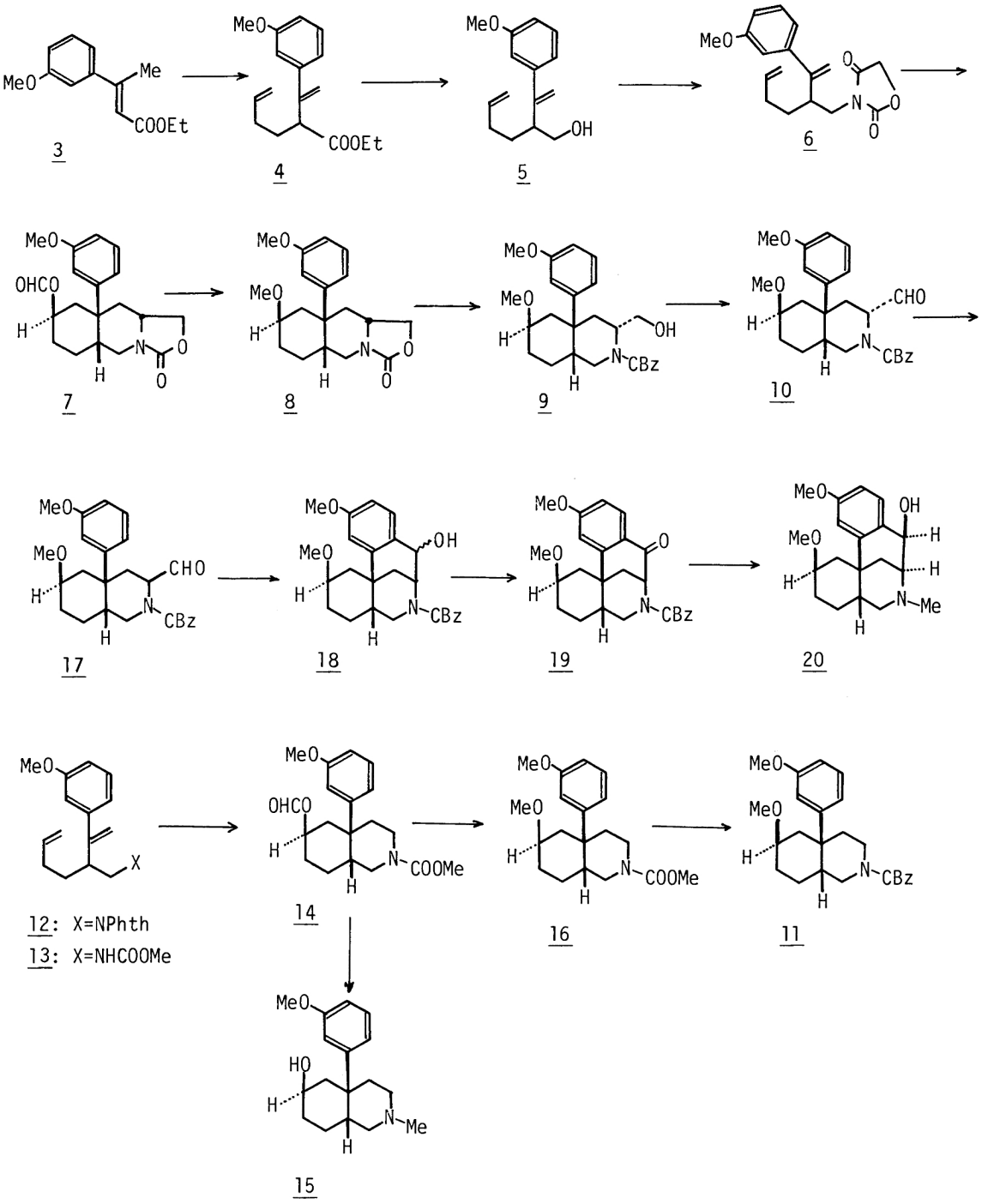


2

α-Butenylation of the ester (3) (LDA, 1-iodo-3-butene, THF, -78 °C ⟶ 20 °C) gave the ester (4),[6] bp 155 °C (2 Torr), in 80% yield, reduction of which ($LiAlH_4$, Et_2O, 0 °C, 2 h) yielded the alcohol (5) as an oil in 82.5% yield. Condensation of 5 with oxazolidine-2,4-dione by Mitsunobu's method[7] gave 6 as an oil in 92% yield. Reduction of 6 (DIBAH, Et_2O, -78 °C), followed by cyclization with formic acid gave the tricyclic isoquinoline (7),[6] mp 149-151 °C, in 68% yield as a single diastereomer. Hydrolysis of 7 (3M NaOH-MeOH, room temperature, 1 h), followed by methylation (NaH, DMF, CH_3I) afforded 8,[6] mp 136-138 °C, in 62% yield. Hydrolysis of 8 (15 equiv. KOH-EtOH, reflux), followed by benzyloxycarbonylation with benzyl chloroformate afforded 9 as an oil in 94% yield. Swern oxidation[8] of 9 (Me_2SO, Et_3N, oxalyl chloride) gave 10[6] as an oil in 94% yield. In order to confirm the ring-juncture and the relative configuration at the 6-position of 10, decarbonylation of 10 with $(Ph_3P)_3RhCl$[9] was carried out to give 11, as an oil, in 52% yield, which was identified with the authentic specimen


MeO
Me
COOEt
3
4
5
6
OHCO
H
N
O
7
8
OH
CBz
9
CHO
10
17
18
19
20
OH
Me
12: X=NPhth
13: X=NHCOOMe
X
COOMe
14
16
11
HO
15

alternatively prepared as follows.

Condensation of 5 with phthalimide by Mitsunobu's method[7] gave 12. Decomposition of 12 with hydrazine hydrate, followed by methoxycarbonylation with methyl chloroformate yielded 13 as an oil in 67% yield. Cyclization of 13 with paraformaldehyde in formic acid gave 14[6] as an oil in 62% yield as a single diastereomer. Reduction of 14 ($LiAlH_4$, THF, 25 °C, 12 h) gave 15, mp 95-97 °C (lit.[10] 95-97 °C), in 83% yield, the spectral data of which were identical with those of the authentic specimen[10] in all respects and not identical with those of the other three diastereomers. The four diastereomers can be easily distinguished by comparison with their physical data.[10] Thus, the stereochemistry of 14 was clearly established as 4a,6-cis-4a,8a-cis. Then 14 was converted to 11 through the usual way via 16. This high diastereoselective cis-ring closure can be accounted for by the significant A-type strain in the monocyclized cationic intermediate.[5,11] Furthermore, the relative configuration at the 3-position of 10 was deduced as 3,4a-trans by the facts that any attempt to cyclize 10 was not successful, although the cyclization smoothly occurred in the case of the epimerized 3-formylisoquinoline (17).

Epimerization at the 3-position in 10 was carried out by treatment with t-BuOK (1 equiv., Et_2O, -5 °C) to give 17[6] as an oil in 72% yield. Apparently, epimerization proceeded through enolation and concomitant protonation procedure. The epimerization at the 3-position is not surprizing in line with the A-strain ideas.[11,12] and it is known that an A-strain can pit agaist 1,3-interaction.[11] Two sets of characteristic signals were observed in the ^1H NMR spectrum of 17. This might be caused by inhibition of free rotation of phenyl and formyl group owing to 1,3-interaction. Cyclization of 17 ($BF_3 \cdot Et_2O$, CH_2Cl_2, 0 °C, 1 min), followed by oxidation of 18 with Jones reagent gave 19[6] as an oil in 60% yield. Aromatic proton signals in its ^1H NMR spectrum indicated that cyclization occurred at the para-position of OCH_3 group. On reduction of 19 with $LiAlH_4$, hydride attacked from the less hindered side to give 20,[6] mp 159-162 °C, in 98% yield, with high diastereoselectivity.

References

1) Reviews on polyene cyclizations: W. S. Johnson, Acc. Chem. Res., 1, 1 (1968); E. E. van Tamelen, ibid., 8, 152 (1975); W. S. Johnson, Bioorg. Chem., 5, 51 (1976); P. A. Bartlett, "Asymmetric Synthesis," ed By J. D. Morrison, Academic Press Inc., New York (1984), Vol. 3, pp. 341-409.

2) M. B. Groen and F. G. Zeelen, J. Org. Chem., 43, 1961 (1978); J. A. M. Perters, T. A. Posthumus, N. P. van Vliet, F. J. Zeelen, and W. S. Johnson, ibid., 45, 2208 (1980); W. S. Johnson, D. Brener, D. J. Dumas, P. J. R. Nederlof, and J. Welch, J. Am. Chem. Soc., 104, 3508 (1982); M. Nishizawa, H. Tanaka, and Y. Hayashi, ibid., 107, 522 (1985).

3) W. N. Speckamp, Recl. Trav. Chim. Pays-Bas, 100, 345 (1981); D. J. Hart and K. Kanai, J. Am. Chem. Soc., 105, 1255 (1983); A. R. Chamberlin and J. Y. L. Chung, ibid., 105, 3653.

4) J. Dijkink and W. N. Speckamp, Tetrahedron, 34, 173 (1978); J. Dijkink and W. N. Speckamp, Tetrahedron Lett., 1977, 935.

5) S. Kano, T. Yokomatsu. Y. Yuasa, and S. Shibuya, J. Org. Chem., 50, 3449 (1985), and references cited therein; S. Kano, T. Yokomatsu, H. Nemoto, and S. Shibuya, ibid., in press.

6) All new compounds gave satisfactory microanalyses, IR, ^{1}H NMR (90 MHz), and Mass spectral data. Selected spectral data are as follows. Only characteristic signals were given for ^{1}H NMR spectra.

7: m/e 345 (M^+), IR ($CHCl_3$) 1750, 1725 cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 3.20 (1H, dd, J=3 and 15 Hz), 3.52 (1H, broad d, J=15 Hz), 3.57-4.03 (1H, m), 3.90 (1H, dd, J=6 and 8 Hz), 4.30 (1H, dd, J=8 and 8 Hz), 5.07 (1H, m, $W_{1/2}$= 28 Hz), 6.80 (1H, dd, J=2 and 8 Hz), 6.91 (1H, d, J=2 Hz), 6.97 (1H, d, J=8 Hz), 7.30 (1H, dd, J=8 and 8 Hz), 7.92 (1H, s).

8: m/e 331 (M^+), IR ($CHCl_3$) 1750 cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 3.21 (1H, dd, J=4 and 15 Hz), 3.30 (3H, s), 3.53 (1H, broad d, J=15 Hz), 3.82 (3H, s), 3.97 (1H, dd, J=6 and 8 Hz), 4.37 (1H, dd, J=8 and 8 Hz), 6.87 (1H, dd, J=2 and 8 Hz), 6.99 (1H, d, J=2 Hz), 7.03 (1H, d, J=8 Hz), 7.39 (1H, dd, J=8 and 8 Hz), ^{13}C NMR ($CDCl_3$) δ 25.4 (t), 31.5 (t), 33.0 (t), 36.96 (d), 41.9 (s), 42.7 (t), 48.1 (t), 51.0 (d), 55.17 (q), 56.64 (q), 67.6 (t), 75.12 (d), 110.5 (d), 112.8 (d), 117.8 (d), 130.0 (d), 146.7 (s), 157.5 (s), 160.1 (s).

10: m/e 437 (M^+), IR ($CHCl_3$) 1730, 1690 cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 3.20 (1H, dd, J=3 and 15 Hz), 3.24 (3H, s), 3.20-3.51 (1H, m), 3.51-3.74 (2H, m), 3.78 (3H, s), 5.08 (2H, s), 6.78 (1H, dd, J=2 and 8 Hz), 6.91 (1H, d, J=2 Hz), 6.96 (1H, d, J=8 Hz), 7.32 (5H, s), 9.52 (1H, d, J=3 Hz).

14: m/e 347 (M^+), ^{1}H NMR ($CDCl_3$) δ 2.76 (1H, d with small spliting, J=12 Hz), 3.05 (1H, dd, J=3 and 12 Hz), 3.68 (3H, s), 3.80 (3H, s), 5.12 (1H, m, $W_{1/2}$= 30 Hz), 6.85 (1H, dd, J=2 and 8 Hz), 6.98 (1H, d, J=2 Hz), 7.02 (1H, dd, J=2 and 6 Hz), 7.35 (1H, dd, J=6 and 8 Hz), 7.98 (1H, s).

17: m/e 437 (M^+), IR ($CDCl_3$) 1740, 1690 cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 3.28 (3H, s), 3.73 (3H, s), 4.46-4.63 (0.4H, m), 4.63-4.81 (0.6H, m), 5.07 (0.8H, s), 5.12 (1.2H, s), 6.74 (1H, dd, J=2 and 8 Hz), 6.84 (1H, d, J=2 Hz), 7.22 (1H, dd, J=8 and 8 Hz), 7.27 (2H, s), 7.33 (3H, s), 8.97 (0.4H, s), 9.00 (0.6H, s).

19: IR ($CHCl_3$) 1700 cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 2.49 (1H, dd, J=4 and 15 Hz), 2.87 (1H, d with small spliting, J=15 Hz), 3.39 (3H, s), 3.86 (3H, s), 4.92 (1H, m), 5.18 (2H, broad s), 6.87 (1H, dd, J=2 and 9 Hz), 6.99 (1H, d, J=2 Hz), 7.35 (5H, broad s), 8.08 (1H, d, J=9 Hz).

20: m/e 317 (M^+), ^{1}H NMR ($CDCl_3$) δ 2.58 (1H, dd, J=5 and 8 Hz), 2.76 (3H, s), 3.10 (1H, broad t, J=5 Hz), 3.27 (3H, s), 3.27-3.77 (2H, m), 3.76 (3H, s), 4.62 (1H, d, J=6 Hz), 6.80 (1H, dd, J=2 and 9 Hz), 6.83 (1H, d, J=2 Hz), 7.50 (1H, d, J=9 Hz).

7) O. Mitsunobu, M. Wada, and T. Sano, J. Am. Chem. Soc., 94, 679 (1972).

8) K. Omura and D. Swern, Tetrahedron, 34, 1651 (1978).

9) J. Tsuji and K. Ohono, Tetrahedron Lett., 1965, 3969.

10) D. D. Weller, R. D. Gless, and H. Rapoport, J. Org. Chem., 42, 1485 (1977).

11) F. Johnson, Chem. Rev., 68, 375 (1968), and references cited therein.

12) von A. Kumin, E. Maverick, P. Seler, N. Vanier, L. Damm, R. Hobi, J. D. Duitz, and A. Eschenmoser, Helv. Chim. Acta, 63, 1158 (1980).

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